

(FILE 'HOME' ENTERED AT 11:22:41 ON 18 JAN 2006)

FILE 'REGISTRY' ENTERED AT 11:22:45 ON 18 JAN 2006

L1           0 S CDTPA OR CTTHA

FILE 'CAPLUS' ENTERED AT 11:22:59 ON 18 JAN 2006

L2           19 S CDTPA OR CTTHA

L3           10 S L2 AND ?IMMUNO?

L4           4 S L3 AND RADIOIMMUNO?

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:204875 CAPLUS  
 DN 141:391080  
 TI Optimization of **radioimmunotherapy** of renal cell carcinoma:  
 labeling of monoclonal antibody cG250 with <sup>131</sup>I, <sup>90</sup>Y, <sup>177</sup>Lu, or <sup>186</sup>Re  
 AU Brouwers, Adrienne H.; Van Eerd, Julliette E. M.; Frielink, Cathelijne;  
 Oosterwijk, Egbert; Oyen, Wim J. G.; Corstens, Frans H. M.; Boerman, Otto  
 C.  
 CS Department of Nuclear Medicine, University Medical Center Nijmegen,  
 Nijmegen, NL-6500 HB, Neth.  
 SO Journal of Nuclear Medicine (2004), 45(2), 327-337  
 CODEN: JNMEAQ; ISSN: 0161-5505  
 PB Society of Nuclear Medicine  
 DT Journal  
 LA English  
 RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT  
 TI Optimization of **radioimmunotherapy** of renal cell carcinoma:  
 labeling of monoclonal antibody cG250 with <sup>131</sup>I, <sup>90</sup>Y, <sup>177</sup>Lu, or <sup>186</sup>Re  
 AB **Radioimmunotherapy** (RIT) can be performed with various  
 radionuclides. We tested the stability, biodistribution, and therapeutic  
 efficacy of various **radioimmunoconjugates** (<sup>131</sup>I, <sup>88</sup>/90Y, <sup>177</sup>Lu,  
 and <sup>186</sup>Re) of chimeric antirenal cell cancer monoclonal antibody G250 (mAb  
 cG250) in nude mice with s.c. renal cell cancer (RCC) tumors. Methods:  
 The <sup>88</sup>/90Y and <sup>177</sup>Lu labeling procedures of cG250 conjugated with cyclic  
 diethylenetriaminepentaacetic acid anhydride (**cDTPA**),  
 isothiocyanatobenzyl-DTPA (SCN-Bz-DTPA), or 1,4,7,10-  
 tetraazacyclododecanetetraacetic acid (DOTA) were characterized.  
 Stability of the labeled conjugates in plasma at 37° was assessed.  
 Biodistribution and therapeutic efficacy of labeled cG250 were compared in  
 nude mice with SK-RC-52 human RCC xenografts. Results: Both SCN-Bz-DTPA  
 and DOTA were stable in vitro (<5% release of the radiolabel during 14 and  
 21 d of incubation) and in vivo (uptake in bone ≤ 1.5 percentage  
 injected dose per g [%ID/g] at 7 d after injection) when used to label <sup>88</sup>Y  
 or <sup>177</sup>Lu to cG250. The DOTA conjugate was slightly but significantly more  
 stable than SCN-Bz-DTPA at 7 d after injection. In vivo, these cG250  
 preps. showed high tumor uptake (70±15 %ID/g ± SD at 7 d after  
 injection). Maximum tumor uptake for <sup>125</sup>I-cG250 and <sup>186</sup>Re-  
 mercaptoacetyltriglycine-(MAG3)-cG250 (<20±3 %ID/g ± SD) was reached  
 at 3 d after injection and was much lower in comparison with cG250 labeled  
 with the residualizing radionuclides. Because the highest specific  
 activities could be prepared using SCN-Bz-DTPA, and relatively low protein  
 doses of cG250 could be administered without saturating the tumor,  
 cG250-SCN-Bz-DTPA conjugates were used in RIT studies. In RIT expts. at  
 maximum tolerated dose, tumor growth was delayed most effectively by cG250  
 labeled with <sup>177</sup>Lu, next most effectively by <sup>90</sup>Y and <sup>186</sup>Re (which were  
 approx. equal), and least by <sup>131</sup>I (delayed by approx. 185, 125, 90, and 25  
 d, resp.). The best median survival (300 d) was observed for  
<sup>177</sup>Lu-SCN-Bz-DTPA-cG250. Median survival for control groups was <150 d.  
 Conclusion: DOTA-conjugated radiolabeled antibodies were the most stable  
**radioimmunoconjugates** in vitro and in vivo as manifested by the  
 lowest bone uptake. However, specific activity was higher for  
 SCN-Bz-DTPA. The RIT studies clearly showed that the therapeutic efficacy  
 of mAb cG250 labeled with <sup>177</sup>Lu, <sup>90</sup>Y, or <sup>186</sup>Re was superior to that of  
<sup>131</sup>I-cG250. The residualizing radionuclides <sup>177</sup>Lu and <sup>90</sup>Y led to higher  
 radiation doses to the tumor and most likely are better candidates than  
 conventionally radiolabeled <sup>131</sup>I for RIT with cG250 in patients with RCC.  
 ST **radioimmunotherapy** renal cell carcinoma; iodine <sup>131</sup>I  
 radiolabeling monoclonal antibody cG250; yttrium <sup>90</sup>Y radiolabeling  
 monoclonal antibody cG250; lutetium <sup>177</sup>Lu radiolabeling monoclonal antibody  
 cG250; rhenium <sup>186</sup>Re radiolabeling monoclonal antibody cG250  
 IT Antibodies and Immunoglobulins  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)  
(monoclonal, labeled, cG250 conjugates; optimization of  
**radioimmunotherapy** of renal cell carcinoma with labeling of  
monoclonal antibody cG250 with 131I, 90Y, 177Lu, or 186Re)

IT Human  
**Immunoradiotherapy**  
(optimization of **radioimmunotherapy** of renal cell carcinoma  
with labeling of monoclonal antibody cG250 with 131I, 90Y, 177Lu, or  
186Re)

IT Kidney, neoplasm  
(renal cell carcinoma; optimization of **radioimmunotherapy** of  
renal cell carcinoma with labeling of monoclonal antibody cG250 with  
131I, 90Y, 177Lu, or 186Re)

IT Carcinoma  
(renal cell; optimization of **radioimmunotherapy** of renal cell  
carcinoma with labeling of monoclonal antibody cG250 with 131I, 90Y,  
177Lu, or 186Re)

IT 67-43-6DP, cyclic, 131I, 90Y, 177Lu, or 186Re complexes 10043-66-0DP,  
Iodine-131, complexes with cG250, biological studies 10098-91-6DP,  
Yttrium-90, complexes with **cDTPA**-cG250, DOTA and SCN-Bz-DTPA,  
biological studies 14265-75-9DP, Lutetium-177, complexes with  
**cDTPA**-cG250, DOTA and SCN-Bz-DTPA, biological studies  
14998-63-1DP, Rhenium-186, complexes with MAG3, cG250, biological studies  
60239-18-1DP, DOTA, 131I, 90Y, 177Lu, or 186Re complexes 66516-09-4DP,  
MAG3, 131I, 90Y, 177Lu, or 186Re complexes 95678-50-5DP, 131I, 90Y,  
177Lu, or 186Re complexes  
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)  
(optimization of **radioimmunotherapy** of renal cell carcinoma  
with labeling of monoclonal antibody cG250 with 131I, 90Y, 177Lu, or  
186Re)

IT 67-43-6, DTPA 10043-66-0, Iodine-131, reactions 10098-91-6,  
Yttrium-90, reactions 14265-75-9, Lutetium-177, reactions 14998-63-1,  
Rhenium-186, reactions 60239-18-1, DOTA 95678-50-5  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(optimization of **radioimmunotherapy** of renal cell carcinoma  
with labeling of monoclonal antibody cG250 with 131I, 90Y, 177Lu, or  
186Re)

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1999:598614 CAPLUS  
DN 132:148530  
TI Pretargeted radio-immunoimaging in ovarian carcinoma  
AU Li, Xiaoping; Feng, Jie; Qian, Henian; Fu, Tianyun; Pang, Yan; Zhu,  
Dianqing; Gao, Baishan  
CS Gynecologic Oncology Center, People's Hospital, Beijing Medical  
University, Beijing, 100044, Peop. Rep. China  
SO Beijing Yike Daxue Xuebao (1999), 31(4), 321-323  
CODEN: BYDXEV; ISSN: 1000-1530  
PB Beijing Yike Daxue  
DT Journal  
LA Chinese  
TI Pretargeted radio-immunoimaging in ovarian carcinoma  
AB The pretargeted **radioimmunoinaging** (RII) technique for improving  
the quality of RII in ovarian carcinoma was established. Monoclonal  
antibody COC183B2 was conjugated with cyclic DPTA (cyclic  
diethylenetriamine pentaacetic acid) DTPA anhydride and its  
**immunoactivity** was measured by **immunohistochem.** or  
autoradiog. in vitro. COC183B2-**cDTPA** or normal mouse IgG  
(NMIgG) were resp. injected i.p. into 2 groups of nude mice bearing human  
ovarian carcinoma with ascites. The reduced 99mTc was injected i.p. again  
48hs later. RII was performed 6hs later. The  $\gamma$  counting of related  
tissues was measured to calculate the ratio of radioactivity for tumor and

non-tumor (T/NT) after RII. The coupled COC183B2 showed good immunoactivity by immunohistochem. and autoradiog. RII showed clear localization of tumor and T/NT ratios were significantly higher than those of the control group 6 h after <sup>99m</sup>Tc administration. Monoclonal antibody COC183B2 coupled by cDTPA used for pretargeted RII is practical, hopefully to be used clin. in ovarian carcinoma.

ST ovarian carcinoma technetium 99m radioimmunoimaging

IT Immunoglobulins

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (G, <sup>99m</sup>Tc-labeled cyclic DTPA conjugates; pretargeted radio-immunoimaging in ovarian carcinoma)

IT Ovary, neoplasm

(carcinoma; pretargeted radio-immunoimaging in ovarian carcinoma)

IT Antibodies

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (monoclonal, labeled; pretargeted radio-immunoimaging in ovarian carcinoma)

IT Imaging

(radioimmunoimaging; pretargeted radio-immunoimaging in ovarian carcinoma)

IT 14133-76-7D, Technetium-99, complex with cyclic DTPA-antibody conjugate, biological studies 23911-26-4D, <sup>99m</sup>Tc-labeled antibody conjugates

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (pretargeted radio-immunoimaging in ovarian carcinoma)

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1996:664588 CAPLUS

DN 125:296522

TI Assessment of Radiochemical Design of Antibodies Using an Ester Bond as the Metabolizable Linkage: Evaluation of Maleimidoethyl 3-(Tri-n-butylstannyl)hippurate as a Radioiodination Reagent of Antibodies for Diagnostic and Therapeutic Applications

AU Arano, Yasushi; Wakisaka, Kouji; Ohmono, Yoshiro; Uezono, Takashi; Akizawa, Hiromichi; Nakayama, Morio; Sakahara, Harumi; Tanaka, Chiaki; Konishi, Junji; Yokoyama, Akira

CS Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-01, Japan

SO Bioconjugate Chemistry (1996), 7(6), 628-637

CODEN: BCCHES; ISSN: 1043-1802

PB American Chemical Society

DT Journal

LA English

AB Reduction of radioactivity levels in nontarget tissues such as the liver and kidney constitutes a problem to be resolved in diagnostic and therapeutic applications of radiolabeled monoclonal antibodies (mAbs). A new radioiodination reagent with an ester bond to liberate m-iodohippuric acid from covalently conjugated proteins, maleimidoethyl 3-(tri-n-butylstannyl)hippurate (MIH), was recently developed. MIH liberated m-iodohippuric acid from galactosylneoglycoalbumin in murine liver, and the radiometabolite was rapidly eliminated from the liver into urine as an intact structure. In this study, intact IgG and Fab fragment of a mAb against osteogenic sarcoma were radioiodinated with MIH to further assess the applicability of MIH to radio-immunoimaging and therapy. For comparison, a mAb radioiodinated with N-succinimidyl iodobenzoate (SIB) and indium-111 (<sup>111</sup>In)-labeled mAbs with diethylenetriaminepentaacetic dianhydride (cDTPA) or 1-[4-[(5-maleimidopentyl)amino]benzyl]EDTA (EMCS-Bz-EDTA) were used. Size-exclusion HPLC anal. and cell binding assays indicated the preservation of both structure and antigen binding affinity of radioiodinated MIH-OST7 (IgG). In biodistribution studies in mice,

[125I]MIH-OST7 (IgG) showed faster systemic clearance of radioactivity after 24 h postinjection than did [131I]SIB- and [111In]EMCS-Bz-EDTA-OST7 (IgG). [125I]MIH-OST7 (IgG) also exhibited much lower radioactivity levels in nontarget tissues such as the liver and kidney, with higher radioactivity levels in the blood up to 72 h postinjection when compared with [111In]cDTPA-OST7 (IgG). Radioactivity excreted from the mice was found in the urine as m-iodohippuric acid, following administration of [125I]MIH-OST7 (IgG). In athymic mice bearing osteogenic sarcoma, [131I]MIH-OST7 (IgG) indicated higher tumor-to-nontarget ratios of radioactivity at both 24 and 48 h postinjection than [125I]SIB-OST7 (IgG). Although both radioiodinated OST7s showed similar radioactivity levels in the target at 24 h postinjection, a small but significant decrease in the target radioactivity level was observed with [131I]MIH-OST7 (IgG) at 48 h postinjection. In addition, [131I]MIH-OST7 (Fab) showed very rapid cleavage of the ester bond both in vivo and in vitro. These findings indicated that while MIH may be a useful reagent for radioimmunoimaging using IgG mAb, its application to smaller mol. weight mAbs and radioimmuno-therapy would be hindered due to the labile characteristics of the ester bond in plasma. Thus, while the present study reinforced the usefulness of metabolizable linkages for reducing nontarget radioactivity levels, a development of plasma-stable metabolizable linkages is also warranted for radioimmuno-therapy and for smaller mol. weight polypeptides.

AN 1994:503190 CAPLUS  
DN 121:103190  
TI Distribution of <sup>111</sup>In- and <sup>125</sup>I-labeled monoclonal antibody 17-1A in mice bearing xenografts of human pancreatic carcinoma HuP-T4  
AU Maeda, Masatoshi; Shoji, Miki; Kawagoshi, Toshiyuki; Futatsuya, Ryusuke; Honda, Takashi; Brady, Luther W.  
CS Fac. Med., Toyama Med. Pharm. Univ., Toyama, 930-01, Japan  
SO Cancer (New York, NY, United States) (1994), 73(3, Suppl.), 800-7  
CODEN: CANCAR; ISSN: 0008-543X  
DT Journal  
LA English  
AB The prognosis of pancreatic adenocarcinoma still remains poor because of the lack of reliable diagnostic tests for early stages of the disease. Monoclonal antibody 17-1A (MoAb 17-1A) has been studied extensively, and the antigen recognized by MoAb 17-1A is expressed by adenocarcinomas of the pancreas and stomach, as well as other normal and malignant epithelial tissues. The potential of MoAb 17-1A was investigated for its ability to detect pancreatic carcinomas. The use of MoAb 17-1A in treatment also was studied. The immunoreactivity of MoAb 17-1A with human pancreatic carcinoma cell line huP-T4 was examined histochem. by the avidin-biotinylated enzyme complex method. MoAb 17-1A was labeled with <sup>125</sup>I by the Iodogen method and <sup>111</sup>In using either diethylenetriaminepentaacetic anhydride (cDTPA) or 1-(p-benzylidiazonium) diethylenetriaminepentaacetic acid (aDTPA). After injection in nude mice bearing HuP-T4 xenografts, the biodistribution of <sup>111</sup>In- and <sup>125</sup>I-labeled MoAb 17-1A was examined at various time points. Pos. staining of MoAb 17-1A was noted for HuP-T4 cells. A statistically significant greater tumor uptake was observed at 3 days after i.v. injection of <sup>125</sup>I-labeled MoAb 17-1A when compared with <sup>125</sup>I-labeled nonspecific IgG. <sup>125</sup>I- and <sup>111</sup>In-labeled MoAb 17-1A was concentrated in HuP-T4 carcinoma 1.9-4.8 times higher than in the spleen, heart, liver, and pancreas. MoAb 17-1A was found to bind selectively to human pancreatic carcinoma HuP-T4. Tumor exhibited higher uptake of radiolabeled MoAb 17-1A compared with adjacent normal tissues. These results suggest that MoAb 17-1A may be applicable to the radioimmunodetection and radioimmunotherapy of pancreatic adenocarcinomas.

(FILE 'HOME' ENTERED AT 11:22:41 ON 18 JAN 2006)

FILE 'REGISTRY' ENTERED AT 11:22:45 ON 18 JAN 2006

L1 0 S CDTPA OR CTTHA

FILE 'CAPLUS' ENTERED AT 11:22:59 ON 18 JAN 2006

L2 19 S CDTPA OR CTTHA

L3 10 S L2 AND ?IMMUNO?

L4 4 S L3 AND RADIOIMMUNO?

=> s l2 not l4

L5 15 L2 NOT L4

=> d bib abs 1-15

L5 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:903042 CAPLUS

DN 143:40064

TI In vitro detection of mdrl mRNA in murine leukemia cells with  
111In-labeled oligonucleotide

AU Bai, Jingming; Yokoyama, Kunihiro; Kinuya, Seigo; Shiba, Kazuhiro;  
Matsushita, Ryo; Nomura, Masaaki; Michigishi, Takatoshi; Tonami, Norihisa

CS Department of Biotracer Medicine (Nuclear Medicine), Kanazawa University  
Graduate School of Medical Sciences, Kanazawa, 920-8640, Japan

SO European Journal of Nuclear Medicine and Molecular Imaging (2004), 31(11),  
1523-1529

CODEN: EJNMA6; ISSN: 1619-7070

PB Springer GmbH

DT Journal

LA English

AB Purpose: The feasibility of intracellular mdrl mRNA expression detection with radiolabeled antisense oligonucleotide (ODN) was investigated in the murine leukemia cell line, P388/S, and its subclonal, adriamycin-resistant cell line, P388/R. Methods: The expression level of mdrl mRNA was analyzed by reverse transcription-polymerase chain reaction (RT-PCR). Existence of the multidrug resistance (MDR) phenomenon was assessed via cellular uptake of 99mTc-sestamibi (MIBI), a known substrate for P-glycoprotein. A 15-mer phosphorothioate antisense ODN complementary to the sequences located at -1 to 14 of mdrl mRNA and its corresponding sense ODN were conjugated with the cyclic anhydride of diethylene triamine penta-acetic acid (cDTPA) via an amino group linked to the terminal phosphate at the 5' end at pH 8-9. The DTPA-ODN complexes at concns. of 0.1-17.4  $\mu$ M were reacted with 111InCl3 at pH 5 for 1 h. The hybridization affinity of labeled ODN was evaluated with size-exclusion high-performance liquid chromatog. following incubation with the complementary sequence. Cellular uptake of labeled ODN was examined in vitro. Furthermore, enhancing effects of synthetic lipid carriers (Transfast) on transmembrane delivery of ODN were assessed. Results: P388/R cells displayed intense mdrl mRNA expression in comparison with P388/S cells. 99mTc-MIBI uptake in P388/S cells was higher than that in P388/R cells. Specific radioactivity up to 1,634 MBq/nmol was achieved via elevation of added radioactivity relative to ODN molar amount. The hybridization affinity of antisense 111In-ODN was preserved at approx. 85 irresp. of specific activity. Cellular uptake of antisense 111In-ODN did not differ from that of sense 111In-ODN in either P388/S cells or P388/R cells. However, lipid carrier incorporation significantly increased transmembrane delivery of 111In-ODN; moreover, specific uptake of antisense 111In-ODN was demonstrated in P388/R cells. Conclusion: Radiolabeling of ODN at high specific radioactivity and specific uptake of antisense 111In-ODN in drug-resistant cells may facilitate future gene

imaging of mdrl mRNA.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:501628 CAPLUS

DN 142:34717

TI Labelling and control of biomolecules with 188Re and 153Sm

AU Balter, H. S.; Verdera, E. S.; Rodriguez, G.; Oliver, P.; Souto, B.; Mallo, L.; Robles, A.

CS Departamento de Radiofarmacia, Centro de Investigaciones Nucleares, Montevideo, Urug.

SO International Atomic Energy Agency, [Technical Document], IAEA-TECDOC (2003), IAEA-TECDOC-1359, Labeling Techniques of Biomolecules for Targeted Radiotherapy, 183-195

CODEN: IAEIE2; ISSN: 1011-4289

DT Report

LA English

AB The aim of this work was to develop and/or standardize the labeling of different biomols. with beta emitters as well as their radiochem. and biol. quality control methods. Lanreotide was labeled with 188Re with yields >90% with good stability using SnF2 in the presence of ascorbic acid and HEDP (molar ratio HEDP/lanreotide=260 and SnF2/lanreotide=40) at pH 1-2. In order to conduct indirect labeling, the synthesis of 188Re-MAG3-TFP ester was done. Lanreotide was also labeled with 125I by chloramine-T method and Bolton-Hunter method with yield >95% and RCP >98% after purification. Somatostatin receptors from rat brain cortex were prepared, their control with 125I-somatostatin gave maximum binding capacity near to 100%. 188Re-lanreotide binding was low and could be inhibited with unlabeled lanreotide but not with somatostatin. 153Sm-EB1 was obtained with RCP >90%, without affecting the binding site for avidin-biotin complex using molar ratio EB1-153Sm 20:1, at 80°C, 10 min. Conjugation of 83D4 and IgG bovine with cDTPA was done and labeled with 153Sm (yield <20%). Radioiodination (chloramine-T method) of native and biotinylated 83D4, scFv and VH with BMCC-biotin in 1:50, 1:25 and 1:25 molar ratios resp., were achieved with yields >50%. Their binding capacity with respect to Tn structure and avidin by immunoradiochem. anal. and by formation of triple complex [AcB]-[avidin]-[111In-DTPA-biotin] was higher for 83D4 than for the recombinant fragments: %B/T=36 for native and %B/T=38 for 83D4-biotin. The highest affinity constant, determined by surface plasmon resonance, was obtained

for 83D4-biotin, KA=1+1010 M-1, while the value for the 83D4 was 7+109 M-1. In order to gain experience and then switch to therapeutic applications by replacing 99Tcm with 188Re, the labeling conditions of 99Tcm-N4-Lys-Biotin were investigated. The best results were obtained using 50 µg of the ligand (61 µmol), 50 µg of SnCl2 (224 µmol) at pH 12, incubating a RT. A diagnostic study in a patient with colon carcinoma by using a pretargeting system showed the location of the tumor at 2 h and a predominant renal excretion of the labeled mol. Bifunctional chelating agents cDTPA and TETA were synthesized.

L5 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:619147 CAPLUS

DN 136:213105

TI A practical approach to glomerular filtration rate measurements:

Creatinine clearance estimation using cimetidine

AU Serdar, Muhittin A.; Kurt, Ismail; Ozcelik, Fatih; Urhan, Muammer; Ilgan, Seyfettin; Yenicesu, Mujdat; Kenar, Levent; Kutluay, Turker

CS Departments of Clinical Biochemistry, Gulhane School of Medicine, Ankara, 06018, Turk.

SO Annals of Clinical and Laboratory Science (2001), 31(3), 265-273



CODEN: ACLSCP; ISSN: 0091-7370  
PB Association of Clinical Scientists  
DT Journal  
LA English

AB Determination of creatinine clearance (Ccr) is not a reliable indicator of glomerular filtration rate (GFR), owing to tubular secretion of creatinine. It has been reported that Ccr measurements can approx. true GFR after cimetidine (Ci) administration. In this study, GFR was estimated by Cockcroft and Gault's equation (CC-G) based on measurement of plasma creatinine, and Ccr was determined by the standard clearance equation using 4-

and

24-h urine samples (Ccr4 and Ccr24, resp.) in 17 patients and 10 healthy controls. After cimetidine administration (800 mg, 3 times daily), GFR values were recalcd. at the same time periods (CCiC-G, CcrCi4 and CcrCi24, resp.). The results were all compared to those obtained by the 99mTc-DTPA protein-free double-sample method (CDTPA), which is a reference method for GFR determination. The coefficient of variation (CV%) for Ccr24/CDTPA was high before cimetidine administration; Ccr24 and CcrCi24 values were significantly different from CDTPA (CV 23.1%, Ccr24/CDTPA = 1.17, p 0.005; and CV 14.1%, CcrCi24/CDTPA = 0.92, p 0.006, resp.). Ccr4 values obtained before cimetidine ingestion showed large variation and were significantly different from CDTPA (CV 15.5%, Ccr4/CDTPA = 1.11, p 0.001). CcrCi4 values after cimetidine were similar to CDTPA (CV 6.9%, CcrCi4/CDTPA = 1.01, p 0.28). CC-G ests. were higher before cimetidine intake (CV 12.4%, CC-G/CDTPA = 1.21, p <0.001), whereas CCiC-G values were not significantly different from CDTPA values (CV 7.0%, CCiC-G/CDTPA = 1.01, p 0.67). This study shows that GFR estns. by CC-G, Ccr4, Ccr24, or CcrCi24 are insufficiently reliable. On the other hand, CCiC-G and CcrCi4 results are acceptable for true GFR estns.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1999:753947 CAPLUS  
DN 132:152633

TI Determination of structural and electrical parameters for activated composite membranes containing di-(2-ethylhexyl)dithiophosphoric acid as carrier

AU Oleinikova, Maria; Munoz, Maria; Benavente, Juana; Valiente, Manuel  
CS Facultad de Ciencias, Departamento de Quimica Analitica, Universidad Autonoma de Barcelona, Bellaterra, Barcelona, E-08193, Spain

SO Analytica Chimica Acta (2000), 403(1-2), 91-99  
CODEN: ACACAM; ISSN: 0003-2670

PB Elsevier Science B.V.

DT Journal

LA English

AB The physicochem. characteristics were studied of activated composite membranes (ACMs) of polysulfone membranes with di-2-ethyl-hexyldithiophosphoric acid (DTPA) as carrier. The polysulfone membranes, Udel P-3500 were obtained by phase inversion and were cast from N,N-dimethylformamide; a thin top layer of polyamide containing DTPA was obtained by interfacial polymerization of 1,3-phenylenediamine with ACM and

also

contains DTPA. Thus, the final membrane is composed of polyamide and polysulfone layers containing the carrier. The amount of carrier incorporated in the ACM is directly proportional to the concentration of carrier in the casting solution. The distribution dependency can serve as calibration graph applicable for pre-calcn. of extractant concentration in the casting solution

to

manufacture an ACM with a given carrier content. The carrier distribution in the membrane was determined by x-ray microanal. (EDS); only a limited concentration of

carrier can be incorporated into the top polyamide membrane layer, resulting in redistribution of the excess of extractant along the polymeric structure of the membrane. These results also correlate with those obtained by impedance spectroscopy measurements. The equivalent circuits associated with the different membrane samples agree with a two-layer model for the ACM containing a high concentration of carrier (CDTPA 0.5 M), which allows for the location of a larger amount of carrier into the polyamide layer. The results obtained by the indicated techniques are in good agreement with each other, and provide for the structural characterization of the membrane. The membranes are of interest for selective separation of metals from, e.g., hydrometallurgical effluents.

RE.CNT 26      THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5      ANSWER 5 OF 15    CAPLUS    COPYRIGHT 2006 ACS on STN  
AN      1999:151084    CAPLUS  
DN      130:308460

TI      Pharmacokinetic evaluation of biodistribution data obtained with  
radiolabeled proteins in mice  
AU      Nishikawa, Makiya; Staud, Frantisek; Takemura, Shigeo; Takakura,  
Yoshinobu; Hashida, Mitsuru  
CS      Department of Drug Delivery Research, Graduate School of Pharmaceutical  
Sciences, Kyoto University, Kyoto, 606-8501, Japan  
SO      Biological & Pharmaceutical Bulletin (1999), 22(2), 214-218  
CODEN: BPBLEO; ISSN: 0918-6158  
PB      Pharmaceutical Society of Japan  
DT      Journal  
LA      English

AB      Radiolabeling of proteins is a widely used approach to study their in vivo disposition patterns. However, the obtained results may largely depend on the radiolabeling method used. The purpose of the present study was to investigate the effect of the radiolabeling method on the pharmacokinetic anal. of liver targeted protein in mice. Galactosylated bovine serum albumin (Gal-BSA) was labeled with <sup>125</sup>I or <sup>111</sup>In, using diethylenetriamine-pentaacetic dianhydride (CDTPA) or 1-(4-isothiocyanobenzyl)EDTA (SCN-Bz-EDTA) as bifunctional chelating agents. The Gal-BSA was then injected in mice by a bolus i.v. injection. Samples of plasma, urine, liver, kidney, intestine and feces were collected at various time intervals and their radioactivity was measured. In none of the samples examined was there any significant difference in radioactivity distribution originating from the radiolabeling methods within 5 min after administration. After this period, <sup>125</sup>I radioactivity in the liver started to decrease significantly faster than that of <sup>111</sup>In, which would indicate the intracellular degradation of the protein. Consequently, the reappearance of trichloroacetic acid (TCA) soluble <sup>125</sup>I radioactivity in the plasma occurred. But whereas the hepatic uptake clearance (CL<sub>liver</sub>) of [<sup>111</sup>In]DTPA-Gal-BSA remained constant during 8h postinjection, the CL<sub>liver</sub> of [<sup>125</sup>I]Gal-BSA at 30 min represented only one eighth of its initial values. The CL<sub>liver</sub> of [<sup>111</sup>In]SCN-Bz-EDTA-Gal-BSA resembled that of [<sup>111</sup>In]DTPA-Gal-BSA within 1 h of the experiment but it started to decline after this interval. The observed discrepancies most probably resulted from the formation of different radiolabeled metabolites in the hepatocytes and their different capability of crossing biol. membranes. Our findings indicate that among the three methods employed, [<sup>111</sup>In]DTPA radiolabeling of Gal-BSA is the most appropriate method to study its tissue disposition.

RE.CNT 19      THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5      ANSWER 6 OF 15    CAPLUS    COPYRIGHT 2006 ACS on STN  
AN      1998:144512    CAPLUS  
DN      128:254669

TI Reassessment of DTPA as a chelating agent for  $^{111}\text{In}$  labeling of proteins: design of a monoreactive DTPA and its application to antibody labeling with  $^{111}\text{In}$

AU Uezono, Takashi; Arano, Yasushi; Ono, Masahiro; Akizawa, Hiromichi; Wakisaka, Kouji; Yokoyama, Akira; Sakahara, Harumi; Konishi, Junji

CS Fac. Pharmaceutical Scis., Kyoto Univ., Japan

SO Men'eki, Shuyo Kaku Igaku (1995), 10(1), 23-28

CODEN: MSKIFX; ISSN: 1342-3967

PB Men'eki, Shuyo Kaku Igaku Kenkyukai

DT Journal

LA Japanese

AB **CDTPA**-OST7 (IgG1 monoclonal antibodies) complex was prepared, labeled with  $^{111}\text{InCl}_3$ , and the pharmacokinetics of the labeled complex were studied in mice and discussed.

L5 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1997:551514 CAPLUS

DN 127:245005

TI Probing the coordination of metal ions by diethylenetriaminepentaacetic acid-conjugated proteins with electrospray ionization mass spectrometry

AU Bennett, Keiryn L.; Sheil, Margaret M.

CS Department of Chemistry, University of Wollongong, Wollongong, 2522, Australia

SO European Mass Spectrometry (1997), 3(3), 233-244

CODEN: EMSPFW; ISSN: 1356-1049

PB IM Publications

DT Journal

LA English

AB Diethylenetriaminepentaacetic acid (DTPA) was covalently linked to L-lysine, the synthetic peptide cGMP protein kinase substrate (cGMP), horse heart myoglobin and the B72.3 monoclonal antibody (MAb) Fab fragment via an acylation reaction using cyclic DTPA anhydride (**CDTPA**). The reaction of **CDTPA** with myoglobin at 10 and 100 fold molar ratios gave rise to the addition of one diethylenetriaminetetraacetic acid (DTTA) group per protein mol. and this was independent of the initial concentration of the protein. We have shown that the modification is readily observed by electrospray ionization mass spectrometry (ESI-MS) and that the coordination of a range of metal ions by the DTTA group can also be easily detected in ESI mass spectra. In addition, hydrolyzed DTPA alone is found to conjugate a range of metal cations in solution and the intensities of the  $[\text{DTPA} - (\text{X} - 1)\text{H}^+ + \text{Mx}^+]$  complexes (where X = the integer value of the charge on the metal ion and M = the metal cation) observed in ESI mass spectra correlate with known solution stabilities of these complexes. This clearly demonstrates the potential of ESI-MS to determine the number of metal

ions

that can be incorporated into a protein via a chelating ligand, which in turn has implications, for example, in generating radiolabeled proteins for use in immunotherapy and immunodiagnosis of carcinomas.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1997:299305 CAPLUS

DN 126:317625

TI Conventional and High-Yield Synthesis of DTPA-Conjugated Peptides: Application of a Monoreactive DTPA to DTPA-D-Phe1-octreotide Synthesis

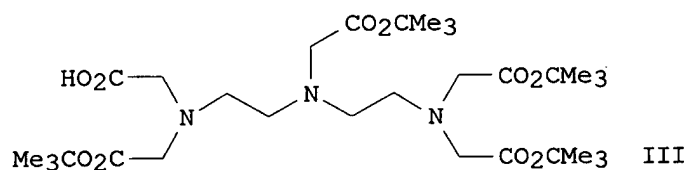
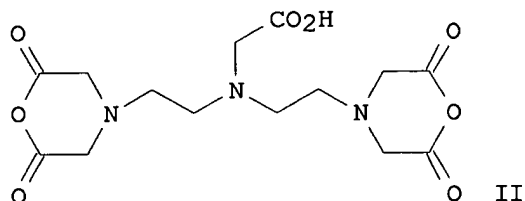
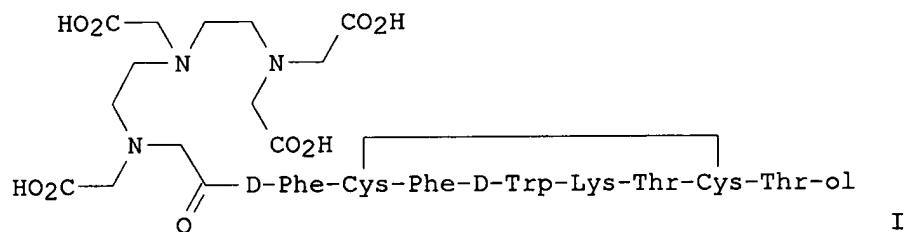
AU Arano, Yasushi; Akizawa, Hiromichi; Uezono, Takashi; Akaji, Kenichi; Ono, Masahiro; Funakoshi, Susumu; Koizumi, Mitsuru; Yokoyama, Akira; Kiso, Yoshiaki; Saji, Hideo

CS Dep. Radiopharm. Chem., Kyoto Univ., Kyoto, 606-01, Japan

SO Bioconjugate Chemistry (1997), 8(3), 442-446

CODEN: BCCHES; ISSN: 1043-1802

PB American Chemical Society  
 DT Journal  
 LA English  
 GI



AB Successful imaging of somatostatin receptor-pos. tumors with  $^{111}\text{In}$ -DTPA-D-Phe<sup>1</sup>-octreotide ( $^{111}\text{In}$ -I) has stimulated development of peptide radiopharmaceuticals using DTPA as the chelating agent. However, use of cyclic DTPA dianhydride II resulted in low synthetic yields of DTPA-peptide by either solution or solid-phase syntheses. This paper reports a novel high-yield synthetic procedure for DTPA-D-Phe<sup>1</sup>-octreotide that is applicable to other peptides of interest using monoreactive DTPA derivative III. Monoreactive DTPA derivative III possesses one free terminal carboxylic acid along with four carboxylates protected with tert-Bu ester (mDTPA) was synthesized. N-9-Fluorenylmethoxycarbonyl-O-tert-butyl-L-threoninol (Fmoc-Thr(tBu)-ol), prepared from Fmoc-Thr(tBu)-OH, was loaded onto 2-chlorotrityl chloride resin. After construction of the peptide chains by Fmoc chemical, mDTPA was coupled to the  $\alpha$  amine group of the peptide on the resin in the presence of 1,3-diisopropylcarbodiimide and 1-hydroxybenzotriazole. Treatment of the mDTPA-peptide-resin with trifluoroacetic acid-thioanisole removed the protecting groups and liberated [Cys(Acm)<sup>2,7</sup>]-octreotide-D-Phe<sup>1</sup>-DTPA from the resin. Iodine oxidation of the DTPA-peptide, followed by the reversed-phase HPLC purification, produced DTPA-D-Phe<sup>1</sup>-octreotide in overall 31.8% yield based on the starting Fmoc-Thr(tBu)-ol-resin. The final product gave a single peak on anal. HPLC, and amino acid anal. and mass spectrometry confirmed the integrity of the product.  $^{111}\text{In}$  radiolabeling of the product provided  $^{111}\text{In}$ -DTPA-D-Phe<sup>1</sup>-octreotide with >95% radiochem. yield, as confirmed by anal. reversed-phase HPLC, TLC, and CAE. These findings indicated that use of mDTPA during solid-phase peptide synthesis greatly increased the synthetic yield of DTPA-D-Phe<sup>1</sup>-octreotide, due to the absence of nonselective reactions that are unavoidable when cDTPA is used. These results also suggested that mDTPA would be a versatile reagent to introduce DTPA with high yield into peptides of interest.

RE:CNT 21      THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5    ANSWER 9 OF 15    CAPLUS    COPYRIGHT 2006 ACS on STN

AN    1996:483602    CAPLUS

DN    125:162256

TI    Reassessment of Diethylenetriaminepentaacetic Dianhydride (DTPA) as a Chelating Agent for Indium-111 Labeling of Polypeptides Using a Newly Synthesized Monoreactive DTPA Derivative

AU    Arano, Yasushi; Uezono, Takashi; Akizawa, Hiromichi; Ono, Masahiro; Wakisaka, Kouji; Nakayama, Morio; Sakahara, Harumi; Konishi, Junji; Yokoyama, Akira

CS    Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-01, Japan

SO    Journal of Medicinal Chemistry (1996), 39(18), 3451-3460

CODEN: JMCMAR; ISSN: 0022-2623

PB    American Chemical Society

DT    Journal

LA    English

AB    Previous studies on indium-111 (<sup>111</sup>In) labeling of polypeptides and peptides using cyclic diethylenetriaminepentaacetic dianhydride (**cDTPA**) as a bifunctional chelating agent (BCA) have indicated that DTPA might be a useful BCA for <sup>111</sup>In labeling of polypeptides at high specific activities when DTPA can be incorporated without inducing intra- or intermol. crosslinking. To investigate this hypothesis, a monoreactive DTPA derivative with a maleimide group as the peptide binding site (MDTPA) was designed and synthesized. A monoclonal antibody (OST7, IgG1) was used as a model polypeptide, and conjugation of MDTPA with OST7, <sup>111</sup>In radiolabeling of MDTPA-OST7, and the stability of <sup>111</sup>In-MDTPA-OST7 were investigated using **cDTPA** and benzyl-EDTA derivs. as refs. SDS-PAGE anal. demonstrated that while **cDTPA** induced intramol. crosslinking, no such undesirable side reactions were observed with MDTPA. MDTPA generated <sup>111</sup>In-labeled OST7 with high radiochem. yields at higher specific activities than those produced using **cDTPA** and benzyl-EDTA derivs. as the BCAs. Incubation of each <sup>111</sup>In-labeled OST7 in human serum indicated that MDTPA generated <sup>111</sup>In-labeled OST7 of much higher and a little lower stability than those derived from **cDTPA** and benzyl-EDTA derivs., resp. These findings indicated that the low in vivo stability of **cDTPA**-conjugated antibody reported previously is not attributable to low stability of <sup>111</sup>In-DTPA but to formation of intramol. crosslinking during **cDTPA** conjugation reactions. The present study also indicated that MDTPA and its precursor, the tetra-tert-Bu derivative of DTPA, would be useful BCAs for <sup>111</sup>In radiolabeling of polypeptides that have rapid blood clearance with high specific activities.

L5    ANSWER 10 OF 15    CAPLUS    COPYRIGHT 2006 ACS on STN

AN    1995:260520    CAPLUS

DN    122:75575

TI    Effect of metabolism on retention of indium-111-labeled monoclonal antibody in liver and blood

AU    Kinuya, Seigo; Jeong, Jae Min; Garmestani, Kayhan; Saga, Tsuneo; Camera, Luigi; Brechbiel, Martin W.; Gansow, Otto A.; Carrasquillo, Jorge A.; Neumann, Ronald D.; Paik, Chang H.

CS    Warren G. Magnuson Clinical Center and Radiation Oncology Branch, National Cancer Institute, Bethesda, MD, 20892, USA

SO    Journal of Nuclear Medicine (1994), 35(11), 1851-7

CODEN: JNMEAQ; ISSN: 0161-5505

DT    Journal

LA    English

AB    The effect of a chelator structure on the metabolic fate of the <sup>111</sup>In-labeled monoclonal antibody (Mab) T101 was investigated in normal Balb/c mice to assess the importance of this chemical parameter in the reduction

of the background radioactivity in blood and liver. Mab T101 was conjugated with either 2-(p-isothiocyanatobenzyl)-6-methyl-diethylaminetriaminepentaacetic acid (DTPA) (1B4M), 2-(p-isothiocyanatobenzyl) cyclohexyl-DTPA (CHX-B) or cyclic DTPA dianhydride (**cDTPA**) and then radiolabeled with <sup>111</sup>In. Normal mice were injected i.v. with these <sup>111</sup>In-labeled T101 conjugates and sacrificed in groups of five up to 5 days postinjection for comparative biodistribution studies and analyses of liver, blood and urine samples for radioindium products. The biodistribution of <sup>111</sup>In-1B4M-T101 and <sup>111</sup>In-CHX-B-T101 were similar to each other but significantly different from that of <sup>111</sup>In-**cDTPA**-T101, particularly in the blood and liver. Size-exclusion high-performance liquid chromatog. indicated that the concentration of the intact <sup>111</sup>In-Ig (lg)G in liver decreased with similar rates for the three conjugates. Meanwhile, the concentration of a small DTPA-like metabolite in liver increased to a different peak value (4.6% ID/g for the **cDTPA** conjugate and 1.6% ID/g for the 1B4M and CHX-B conjugates) approx. at 24 h and maintained a steady-state concentration up to 5 days. The thiourea linkage between T101 and the <sup>111</sup>In-labeled chelates and a higher complex stability and higher lipophilicity of <sup>111</sup>In-1B4M and <sup>111</sup>In-CHX-B appear to be responsible for lower liver and higher blood radioactivity for the 1B4M and CHX-B conjugates.

L5 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1994:696108 CAPLUS

DN 121:296108

TI Comparative biodistributions of indium-111-labeled macrocycle chimeric B72.3 antibody conjugates in tumor-bearing mice

AU Turner, A.; King, D.J.; Farnsworth, A.P.H.; Rhind, S.K.; Pedley, R.B.; Boden, J.; Boden, R.; Millican, T.A.; Millar, K.

CS Celltech R&D, Slough/Berkshire, SL1 4EN, UK

SO British Journal of Cancer (1994), 70(1), 35-41

CODEN: BJCAAI; ISSN: 0007-0920

DT Journal

LA English

AB A novel <sup>111</sup>In ligand (a C-functionalized derivative of 1,4,7-triazacyclononanetriacetic acid), termed 9N3, was covalently attached to chimeric B72.3, labeled with <sup>111</sup>In and compared with <sup>111</sup>In-labeled chimeric B72.3 DTPA cyclic anhydride conjugate (**cDTPA**) and a C-linked derivative of DTPA (CT-DTPA) in athymic mice bearing human colon carcinoma xenografts. Significant differences in biodistribution were observed between 9N3 and **cDTPA** conjugates especially in the tumor uptake and blood, liver, femur and colon levels at 24, 48 and 144 h. Significantly higher tumor uptake was observed for <sup>111</sup>In-cB72.3-9N3 compared with <sup>111</sup>In-cB72.3-**cDTPA** at all time points. Radiolocalization (RI) indexes increased with time for the 9N3 conjugate but remained constant for the **cDTPA** conjugate. The biodistribution of <sup>111</sup>In-labeled cB72.3-CT-DTPA was similar to that of <sup>111</sup>In-labeled cB72.3-9N3 except for elevated kidney levels. A 12N4 macrocycle (a C-functionalized derivative of 1,4,7,10-tetraazacyclododecanetetraacetic acid) was also tested for its ability to chelate <sup>111</sup>In and its biodistribution examined. Labeled conjugates with this macrocycle were more difficult to prepare in a stable form but gave a very similar biodistribution to the 9N3 macrocycle conjugate. Macrocycle-antibody conjugates of this type offer considerable promise for tumor imaging in patients.

L5 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1994:477429 CAPLUS

DN 121:77429

TI Bifunctional chelate agents in <sup>90</sup>Y-labeled antibody - comparison of 1-(p-isothiocyanatobenzyl)-DTPA and cyclic DTPA anhydride

AU Zhang, Jinming; Lin, Qiongfang; Jin, Xiaohai

CS\* China Inst. Ato. Energy, Beijing, 102413, Peop. Rep. China  
 SO He Huaxue Yu Fangshe Huaxue (1993), 15(4), 219-23  
 CODEN: HHHHDH; ISSN: 0253-9950  
 DT Journal  
 LA Chinese  
 AB Two bifunctional chelate agents, 1-(p-isothiocyanatobenzyl)-DTPA (SCN-Bz-DTPA) and cyclic DTPA anhydride (**CDTPA**), are synthesized and conjugated with antibody, subsequently labeled with 90Y (Ac)3. There are differences in the two chelating agents conjugated with antibodies and the radiochem. stability of the preparation in vitro. The results show that SCN-Bz-DTPA is superior to **CDTPA**.

L5 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 1993:164272 CAPLUS  
 DN 118:164272  
 TI The stability in liver homogenates of indium-111 and yttrium-90 attached to antibody via two popular chelators  
 AU Mardirossian, G.; Wu, C.; Hnatowich, D. J.  
 CS Med. Cent., Univ. Massachusetts, Worcester, MA, 01655, USA  
 SO Nuclear Medicine and Biology (1993), 20(1), 65-74  
 CODEN: NMBIEO; ISSN: 0883-2897  
 DT Journal  
 LA English  
 AB To investigate the influence of chelator on the stability in liver homogenates of 111In and 90Y-labeled antibodies, the C110 antibody was conjugated with the cyclic anhydride of DTPA (**CDTPA**) and with isocyanatobenzyl-DTPA (SCN-Bz-DTPA) and labeled with both radionuclides. After incubation in fresh liver homogenates at 37° for 1-2 days, the soluble fraction was analyzed by filtration, HPLC, and TLC to determine the nature and extent of transchelation of the label and catabolism of the antibody. The loss of activity from antibody, as shown by passage through a low mol. weight (10 kDa cut-off) filter, was 3-5-fold more pronounced for 90Y (51 and 68% at 1 and 2 days) than 111In (11 and 29%, resp.). No difference was observed between chelators. Furthermore, anal. of these low mol. weight species showed that even at 1 day, 90Y in contrast to 111In was present as one or more weak complexes and therefore no longer chelated to either DTPA or Bz-DTPA. Little evidence was observed for instability in liver of the thiourea bond whereby SCN-Bz-DTPA is attached to the antibody. By contrast, the identification of 111In-DTPA in the homogenates demonstrates the instability of the amide bond generated by **CDTPA** conjugation. In conclusion, as expected, 90Y was shown to form less stable chelates than 111In; however, in these investigations, the greater denticity of Bz-DTPA over DTPA did not improve stability with either radiolabel.

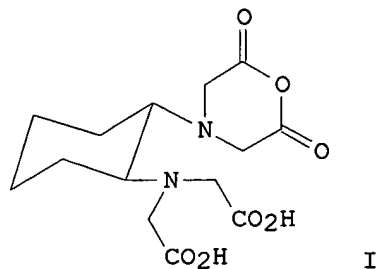
L5 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 1992:2915 CAPLUS  
 DN 116:2915  
 TI Cyclohexyl EDTA monoanhydride for preparation of radiometal-labeled immunoconjugates  
 IN Mease, Ronnie C.; Srivastava, Suresh C.  
 PA Associated Universities, Inc., USA  
 SO U.S., 9 pp.  
 CODEN: USXXAM

DT Patent  
 LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5021571	A	19910604	US 1989-372905	19890629
	US 5089663	A	19920218	US 1991-679258	19910402
	US 5334729	A	19940802	US 1991-787244	19911104

PRAI US 1989-372905 A2 19890629  
 US 1991-679258 A3 19910402  
 OS MARPAT 116:2915  
 GI



AB Title compound I is claimed. I, and the family of new compds. produced by the derivatization of I, are prepared and conjugated to monoclonal antibodies predominantly through lysine groups on the antibody without crosslinking of the antibody. The immunoconjugate formed using the chelating agent produce stable complexes with many radiometals. Many of these complexes are more stable in serum than those formed using non-rigid chelates such as EDTA and DTPA. <sup>111</sup>In-labeled CDTA, trans-**CDTPA**, and trans-**CTTHA** (**CDTPA** = cyclohexyl DTPA; **CTTHA** = cyclohexyl TTHA; preps. given) conjugates with anticolon carcinoma monoclonal antibody 17-1A as well as their nonrigid counterparts EDTA, DTPA, and TTHA were tested in human colon cancer (SW948) xenografted nude mice. The tumor uptake of CDTA and trans-**CTTHA** conjugates was 3-4 times higher than EDTA and TTHA conjugates. They also had slower whole body and blood clearance as well as decreased kidney excretion.

L5 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1987:46564 CAPLUS

DN 106:46564

TI Glomerular filtration assessed by plasma clearance of ytterbium-169--DTPA in kidney recipients. Comparison with inulin, polyfructosan S and creatinine clearance

AU Stribrna, J.; Oppelt, A.; Woller, P.; Franke, W. G.; Jirickova, E.; Janata, V.; Kocandrla, V.; Sup, I.

CS Program Vyzk. Transplant. Organu, Inst. Klin. Exp. Med., Prague, Czech.

SO Casopis Lekarů Ceských (1986), 125(34), 1070-2

CODEN: CLCEAL; ISSN: 0008-7335

DT Journal

LA Czech

AB In 26 recipients of kidney transplants (1-73 mo after the transplantation), plasma clearance of 0.5  $\mu$ Ci <sup>169</sup>Yb-DTPA ( **CDTPA** )/kg (i.v.) determined 4-120 min after the injection was comparable with renal clearance of creatinine (CCR). Renal clearances of inulin or polyfructosan were lower than **CDTPA** or CCR. Distribution rates of radiopharmaceuticals in body compartments and tubular transport of radiopharmaceuticals are discussed in relation to glomerular filtration rates. Thus, **CDTPA** after a single injection of <sup>169</sup>Yb-DTPA and CCR can be used interchangeably for the determination of glomerular filtration rates.

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